Laryngopharyngeal Reflux : Larynx on Fire

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Abstract

Laryngopharyngeal Reflux (LPR) is a commonly occurring and recently described clinical entity due to the retrograde flow of gastric contents into the pharynx. It accounts for many symptoms of upper airway including hoarseness, chronic throat irritation and globus sensation. The sensitive laryngeal mucosa is prone to damage by the combination of acid and pepsin. The inflammatory changes that follow are presumed to cause the symptoms and predispose the individual to laryngeal disorders. Diagnosis can usually be made clinically based on symptoms and laryngeal signs but a 24 hour pH metry is essential to establish diagnosis. Treatment centres on lifestyle modifications, vocal hygiene measures and long term use of proton pump inhibitors. Recent research in this field may lead to a better understanding of the pathophysiology of the disease and change the way LPR is managed.

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Key Words: Laryngopharyngeal reflux; pH metry; Proton pump inhibitors

Introduction

Laryngopharyngeal reflux (LPR) is a recently described clinical entity which is caused due to the retrograde flow of gastric contents into the pharynx. The 'American Academy of Otolaryngology-Head and Neck Surgery' adopted the name "Laryngopharyngeal Reflux" in 2002 and issued a position statement describing the condition [1]. Of late, interest in this distinct entity has grown manifold with a large number of hitherto vague clinical presentations ascribed to this phenomenon. Not only has it been implicated in common presentations like "globus hystericus" but also in the etiology of laryngeal carcinoma. The importance of LPR can be gauged by the suggestion that up to 50% of all patients suffering from hoarseness and voice disorder may have significant LPR [2]. The pathophysiology and diagnostic criterion of this disease have been evolving and general awareness in the medical community is required to correctly treat laryngopharyngeal reflux disease (LPRD). The recent trend to diagnose this pathology has been aptly summarised by Charles Ford who writes that LPR is a major cause of laryngeal inflammation and presents with a constellation of symptoms different from classic gastroesophageal reflux disease (GERD) [3]. This article is meant to be an introduction into the concepts of LPR and written with the general practitioners in mind in order to sensitize them to this issue.

Pathophysiology

The posterior glottis bears the brunt of the upper aerodigestive tract secretions. All streams of mucociliary transport finally join together in the inter-arytenoid area thus making it akin to a 'gutter' for all the secretions. A lot of irritants including allergens, irritants, smoke, alcohol and acidic gastric contents and enzymes bathe this area round the clock. All these secretions and trapped particles from the nose, the lungs and the oral cavity converge here to finally get swallowed. However when the 'gutter' backflows, it brings with it gastric contents containing acid and pepsin harmful to the sensitive laryngeal mucosa. Refluxate from the stomach reaches the hypopharynx and larynx along the esophagus and causes a generalised low degree burn with associated inflammation. What initially causes the inflammatory process to start is difficult to envisage, but what is sure is that in the presence of pepsin in the reflux, the condition worsens and leads to changes that cause symptoms and signs. An international collaborative research group is studying the cellular impact of LPR on laryngeal epithelium. They have reported reduced levels of bicarbonate producing enzyme carbonic anhydrase subtype III in laryngeal epithelium taken from LPR patients compared to high levels in normal laryngeal epithelium [4]. One study has also suggested the role of bile reflux in the causation of LPR [5].

At this stage it is interesting to review the important differences in the pathophysiology of GERD and LPR.

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The esophagus is a dynamic tube that functions to propel contents of the pharynx to the stomach as part of the deglutition process. As the food gets swallowed to the acidic milieu of the stomach, some of these acidic contents intermittently leak out of the physiological lower esophageal sphincter (LES) and enter the esophagus. These episodes are normal and referred to as gastro-esophageal reflux episodes and when they become pathological constitute the GERD. The same is not true of the pharynx and once the refluxate reaches the unprotected laryngeal mucosa it is always pathological and causes damage. Therefore, even a single episode of pH fall in the pharynx is considered significant and diagnostic of LPR. Also in contrast to the nocturnal reflux suffered by the patients of GERD, LPR patients suffer from upright daytime reflux and symptoms.

Clinical picture

Patients suffering from LPR often are a frustrated lot after multiple visits to the doctor has yielded no diagnosis and several courses of antibiotics and antihistamines have been tried. The symptoms themselves are vague and range from a relatively simple hoarseness of voice to an indistinct feeling of globus and chronic throat clearing. This calls for a need of high awareness amongst the medical profession as such symptoms are usually discarded by some doctors as being functional. Of special mention are two scales which attempt to quantify the clinical findings in patients suspected to be suffering from LPR. The first index is the reflux symptom index (RSI) which is a validated self administered questionnaire with nine questions being answered by the patients on a five point scale (Table 1) [6]. Another scale is the reflux finding score (RFS) and this is useful to depict the typical clinical picture of LPR. This is based on a fiberoptic laryngoscopy and findings commonly seen in these patients are recorded on a scale. A score of more than seven is highly suggestive of LPR. A mirror examination is often insufficient to gauge the extent and severity of LPR though the picture may be suggestive. The most common clinical findings on

laryngoscopy are posterior commissure hypertrophy and diffuse edema of the false cords obliterating the ventricular opening. Erythema and thick mucus also are frequently seen. Some typical laryngoscopic findings are depicted in Fig. 1. Total reliance cannot be placed on one laryngeal finding alone and many a normal person may also have one or more similar findings. Also there exists a problem of some degree of inter-physician variability in assessing these findings which makes it difficult to diagnose LPR on the basis of clinical picture alone.

The voice in a case of LPR gets adversely affected and often is the main symptom. An objective analysis of the voice parameters usually reveals a reduction in the pitch range, maximum frequency, phonetogram area and maximum phonation time [7]. In the Indian scenario, admittedly, the availability of such measurements is limited to specialised centres only.

Diagnosing

So if the symptoms are vague and findings suffer from inter-observer bias, how does one reliably diagnose a case of LPR? The diagnosis is based on a background of symptoms and signs with a positive 24 hour pH metry. A 24 hour ambulatory dual-probe pH metry is considered as the 'gold standard' in diagnosing a patient of LPR. Though its availability is limited, it is the only reliable investigation at present which confirms LPR. In this, a single fine tube like channel is positioned in the patient much like a nasogastric tube. This electrode has two pH sensors along its length and the lower one is placed in the lower esophagus approximately five cm above the LES and the upper one in the laryngopharynx. The placement of the electrode may need to be guided by esophageal manometry in select cases. The electrode is attached to a portable data logger which keeps a record of pH measurements, body posture and meal times. After 24 hours of normal routine activity by the patient, the data is analysed using a computer and a 24 hour graph of pH levels studied. Even a single episode of pH < 4 in the laryngopharynx is considered significant.

Table 1

The Reflux Symptom Index, a score of >10 could indicate significant reflux

Within the past month, how did the following problems affect you?	0 = No problem, 5 = Severe problem					
Hoarseness or a problem with your voice	0	1	2	3	4	5
Clearing your throat	0	1	2	3	4	5
Excess throat mucus or feeling of postnasal drip	0	1	2	3	4	5
Difficulty swallowing food, liquids or tablets	0	1	2	3	4	5
Coughing after eating or lying down	0	1	2	3	4	5
Breathing difficulties or choking episodes	0	1	2	3	4	5
Troublesome or annoying cough	0	1	2	3	4	5
Sensations of something sticking in your throat or a lump in your throat	0	1	2	3	4	5
Heartburn, chest pain, indigestion or stomach acid coming up	0	1	2	3	4	5
T o t a l						

Table 2**Vocal Hygiene : A list of do's and don'ts**

Do's	Do Not's
<ul style="list-style-type: none"> • Drink plenty of water (at room temperature) • Speak on a 'as required' basis • Relax when speaking • Steam inhalation • Take a light walk before bedtime • Take small meals • Take any other medications only after showing it to your doctor • Have adequate sleep 	<ul style="list-style-type: none"> • Shout / Whisper. Speak in a low / moderate volume instead • Speak continuously for more than 20 minutes. Take a 20 min break • Clear your throat frequently • Smoke • Consume alcohol • Drink more than 2 cups of tea / coffee per day • Eat oily / spicy food / chocolate / consume aerated drinks

Fig. 1 : Typical laryngeal findings in LPR. Edematous true and false vocal folds, arytenoid congestion, interarytenoid edema and thick endolaryngeal mucus.

A typical LPR episode is classically preceded by an esophageal drop in pH (Fig. 2). Other important parameters include the number of reflux episodes and the acid exposure time. A meta-analysis which tested the role of upper probe measurements across 16 studies and concluded it to be a reliable and consistent method worldwide [8]. Recently probes have been designed for more accuracy (four channels) and better tolerance (aerosol detecting pH probes for oropharyngeal use) [9,10].

Treatment

The mainstay of managing a diagnosed case of LPR is a mix of proton pump inhibitors (PPIs) and lifestyle modifications often called vocal hygiene. Vocal hygiene is a term often misunderstood and open to interpretations. Table 2 lists out the measures we are following in our institute for our patients. The Indian diet is rich in oils and spices and along with their reduction, excessive tea intake needs to be curtailed. Vocal hygiene, if properly practiced, probably helps a large number of patients. Anti reflux pharmacotherapy classically consists of administration of twice daily PPIs (omeprazole,

Fig. 2 : Tracing of a dual probe pH metry showing a laryngeal reflux episode marked by a sudden reduction of pH <4 in the laryngeal probe (red) preceded by the esophageal probe (blue).

lansoprazole, pantoprazole) for a period of minimum three months and extending up to six months in refractory cases. These drugs show significant improvement in both symptoms and local findings with more than 80% patients showing promising response in three months. Some recent evidence has however failed to show similar promise and therefore in our clinical practice, we insist on a positive pH metry finding before commencing PPIs [11,12]. The role of empirical usage of PPIs based on symptoms / symptom scores alone is not recommended as per a systematic review [13]. However, in the Indian scenario where access to pH metry equipment is often non-existent, lifestyle modifications including vocal hygiene measures can safely be advised and proton pump inhibitors used in non-responding cases as a therapeutic trial.

Future trends

Pepsin assay: Evolving a non-invasive test to reliably diagnose LPR has led to research into using examining stomach enzyme pepsin in sputum. The result is the pepsin immunoassay test which promises to be a sensitive and non-invasive method to diagnose LPR [14].

Ultrastructural analysis: A limited Egyptian study has investigated the role of electron microscopic analysis of oropharyngeal mucosa to diagnose LPR. A dilatation

of intercellular spaces used as a morphological marker for LPR has been suggested as a diagnostic aid [15].

Role of surgery: Laparoscopic fundoplication has been described for selected cases of LPR [16]. Being a minimally invasive procedure, this surgery increasingly has become more acceptable. In our setting however we have limited experience in this treatment modality.

Association with laryngeal cancer: One of the hypotheses being researched worldwide is a possible cause effect relationship between LPR and laryngeal malignancy [17]. Such a link would call for paradigm changes in management of laryngeal cancer. Though some ultrastructural and immunological studies of laryngeal mucosa suggest such a link, clinical evidence available is still inconclusive [18].

Association with other diseases: LPR is increasingly being associated with other conditions of the aerodigestive tract including sinusitis, paediatric otitis media with effusion, recurrent otitis media and even sudden infant death syndrome [19, 20]. An association with sleep disordered breathing has often been observed in our patients and some researchers have suggested a vicious cycle between LPR and obstructive sleep apnea [21]. Whether such associations represent a cause-effect relationship will only be clear once the pathogenesis of laryngopharyngeal reflux disease is better understood.

Conclusion

The understanding of the entity of LPR and its manifestations is far from being completely understood. Controversies remain in all spheres of this disease namely the pathophysiology, symptomatology, clinical findings, pH analysis and treatment aspects. With ever increasing research in this field, hopefully some of these questions would be answered. It is important for the ENT surgeon to be fully aware of this condition as LPR presents itself in many ways and is in itself a factor for many other otolaryngological disorders.

Conflicts of Interest

None identified

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